

USSN: 10/677,551

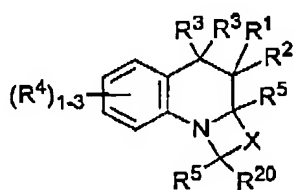
Ref. No. 27712 (formerly 01337.US1)

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of formula I, including enantiomeric, diastereomeric, or tautomeric isomers thereof, or any pharmaceutically acceptable salt thereof;



I

wherein,

R¹ is

- (a) R¹²
- (b) C(=O)R⁶, or
- (c) CN;

R² is

- (a) R¹²
- (b) C(=O)R⁷,
- (c) CN,
- (d) -CH₂-R⁷,
- (e) -NR¹⁷R⁷,
- (f) -CH₂COR⁷,
- (g) -CH₂CH₂COR⁷;

Each R³ is independently

- (a) H,
- (b) R¹²,
- (c) —Oxo,

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(c) ~~(d)~~ C₁₋₇ alkyl which is optionally partially unsaturated and is optionally substituted by one or more R¹¹,

(d) ~~(e)~~ C₃₋₈ cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R¹¹,

(e) ~~(f)~~ aryl optionally substituted by one or more R⁸,

(f) ~~(g)~~ heteroaryl optionally substituted by one or more R⁸, or

(g) ~~(h)~~ halo, or

(h) both R₃ taken together are oxo;

Each R⁴ is independently

- (a) H,
- (b) halo,
- (c) OR¹²,
- (d) OC(=O)NR⁹R¹⁰,
- (e) SR¹²,
- (f) S(O)_mR¹³,
- (g) NR⁹R¹⁰,
- (h) NR⁹S(O)_mR¹³,
- (i) NR⁹C(=O)OR¹³,
- (j) phenyl optionally substituted by one or more R⁸,
- (k) heteroaryl optionally substituted by one or more R⁸,
- (l) cyano,
- (m) nitro,
- (n) CONR⁹R¹⁰,
- (o) CO₂R¹²,
- (p) C(=O)R¹³,
- (q) C(=NOR¹²)R¹³,
- (r) S(O)_mNR⁹R¹⁰,
- (s) NR⁹C(=O)-R¹²,
- (t) C₁₋₇alkyl which is optionally partially unsaturated and is optionally substituted by one or more R¹¹,

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(u) C₃₋₈cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R¹¹,

(v) N₃,

(w) het¹ optionally substituted by one or more R⁸, or

(x) C(O)O-C₁₋₄alkyl-R¹²;

Each R⁵ is independently,

(a) H,

(b) C₁₋₇alkyl which is optionally partially unsaturated and is optionally substituted by one or more R¹¹,

(c) C₃₋₈cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R¹¹,

(d) aryl optionally substituted by one or more R⁸, or

(e) heteroaryl optionally substituted by one or more R⁸;

R⁶ and R⁷ are independently;

(a) OR¹²,

(b) NR⁹R¹⁰,

(c) R¹³, or

(e) R⁶ and R⁷ together with the 2 carbons to which they are attached form cyclohexane-1,3-dione optionally substituted by one or more R¹³, cyclopentane-1,3-dione optionally substituted by one or more R¹³, R⁶ and R⁷ together form -N(R¹⁷)-S(O)_m-N(R¹⁷)-, -N(R¹⁷)-C(O)-N(R¹⁷)-, -N(R¹⁷)-C(S)-N(R¹⁷)-, -N(R¹⁷)-N(R¹⁷)-, -N(R¹⁷)-C(O)-, or -N(R¹⁷)-, or R⁶ and R⁷ together form a phenyl ring;

R⁸ is

(a) H,

(b) halo,

(c) OR¹²,

(d) OCF₃,

(e) SR¹²,

(f) S(O)_mR¹³,

(g) NR⁹R¹⁰,

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- (h) $\text{NR}^9\text{S(O)}_m\text{R}^{13}$,
- (i) $\text{NR}^9\text{C(=O)OR}^{13}$,
- (j) phenyl optionally substituted by halo, cyano, C_{1-7} alkyl, or C_{1-7} alkoxy, in the alkyl portion of the C_{1-7} alkyl and C_{1-7} alkoxy is optionally substituted by one or more R^{11} ;
- (k) heteroaryl optionally substituted by halo, C_{1-7} alkyl, or C_{1-7} alkoxy,
- (l) cyano,
- (m) nitro,
- (n) $\text{CONR}^9\text{R}^{10}$,
- (o) CO_2R^{12} ,
- (p) C(=O)R^{13} ,
- (q) $\text{C(=NOR}^{12})\text{R}^{13}$,
- (r) $\text{S(O)}_m\text{NR}^9\text{R}^{10}$,
- (s) $\text{NR}^9\text{C(=O)-R}^{12}$,
- (t) C_{1-7} alkyl which is optionally partially unsaturated and is optionally substituted by one or more R^{11} ,
- (u) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R^{11} ,
- (v) $-\text{C(O)H}$, or
- (w) $-\text{het}^1$;

R^9 and R^{10} are independently

- (a) H,
- (b) OR^{12} ,
- (c) aryl optionally substituted by one or more R^{14} ,
- (d) heteroaryl optionally substituted by one or more R^{14} ,
- (e) C_{1-7} alkyl which is optionally substituted by one or more R^{11} ,
- (f) C_{3-8} cycloalkyl which is optionally substituted by one or more R^{11} ,
- (g) (C=O)R^{13} , or
- (h) R^9 and R^{10} together with the nitrogen to which they are attached form morpholine, pyrrolidine, piperidine, thiazine, piperazine, each of the morpholine, pyrrolidine, piperidine, thiazine, piperazine being optionally substituted with R^{11} ;

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 R^{11} is

- (a) oxo,
- (b) phenyl optionally substituted by one or more R^{14} ,
- (c) OR^{12} ,
- (d) SR^{12} ,
- (e) $NR^{12}R^{12}$,
- (f) halo,
- (g) CO_2R^{12} ,
- (h) $CONR^{12}R^{12}$,
- (i) C_{1-7} alkyl which is optionally substituted oxo, halo, OR^{12} , SR^{12} , C_{1-7} alkyl, or $NR^{12}R^{12}$ substituents, or
- (j) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more oxo, halo, OR^{12} , SR^{12} , C_{1-7} alkyl, or $NR^{12}R^{12}$ substituents;

 R^{12} is

- (a) H,
- (b) C_{1-7} alkyl which is optionally partially unsaturated and is optionally substituted by oxo, halo, C_{1-7} alkyl, or C_{1-7} alkoxy substituents,
- (c) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more oxo, halo, C_{1-7} alkyl, or C_{1-7} alkoxy substituents,
- (d) aryl optionally substituted by one or more halo, C_{1-7} alkyl, or C_{1-7} alkoxy substituents, or
- (e) heteroaryl optionally substituted by one or more halo, C_{1-7} alkyl, or C_{1-7} alkoxy substituents;

 R^{13} is

- (a) C_{1-7} alkyl which is optionally substituted by one or more by oxo, halo, carboxyl, C_{1-7} alkyl, or C_{1-7} alkoxy substituents,
- (b) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more by oxo, halo, C_{1-7} alkyl, or C_{1-7} alkoxy substituents,
- (c) aryl optionally substituted by one or more halo, C_{1-7} alkyl, or C_{1-7} alkoxy substituents;

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(d) heteroaryl optionally substituted by one or more halo, C₁₋₇alkyl, or C₁₋₇alkoxy substituents,

(e) -C(O)OH

R¹⁴ is

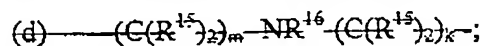
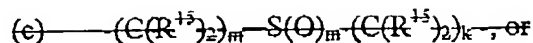
- (a) H,
- (b) halo,
- (c) C₁₋₇alkyl,
- (d) OR¹²,
- (e) OCF₃,
- (f) SR¹²,
- (g) S(O)_mR¹³,
- (h) NR¹²R¹²,
- (i) NR¹²S(O)_mR¹³,
- (j) NR¹²C(=O)OR¹³,
- (k) phenyl optionally substituted by halo, C₁₋₇alkyl, or C₁₋₇alkoxy,
- (l) heteroaryl optionally substituted by halo, C₁₋₇alkyl, or C₁₋₇alkoxy,
- (m) cyano,
- (n) nitro,
- (o) CONR¹²R¹²,
- (p) CO₂R¹²,
- (q) C(=O)R¹³,
- (r) C(=NOR¹²)R¹³,
- (s) S(O)_mNR¹²R¹²,
- (t) NR⁹C(=O)-R¹²,
- (u) C₁₋₇alkyl which is optionally partially unsaturated and is optionally substituted by oxo, halo, OR¹², SR¹², C₁₋₇alkyl, or NR¹²R¹² substituents, or
- (v) C₃₋₈cycloalkyl which is optionally partially unsaturated and is optionally substituted by oxo, halo, OR¹², SR¹², C₁₋₇alkyl, or NR¹²R¹² substituents;

X is

- (a) $\text{---}(\text{C}(\text{R}^{15})_2)_n\text{---}$
- (b) $\text{---}(\text{C}(\text{R}^{15})_2)_m\text{---O---}(\text{C}(\text{R}^{15})_2)_k\text{---}$

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Each R^{15} is independently

- (a) H,
- (b) OR^{11} ,
- (c) Oxo,
- (d) C_{1-7} alkyl which is optionally substituted by one or more ~~by one or~~ R^{11} substituents,

(e) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more ~~by one or more~~ R^{11} substituents,

- (f) aryl optionally substituted by one or more R^8 , or
- (g) heteroaryl optionally substituted by one or more R^8 ;

 R^{16} is

- (a) H
- (b) OR^{12} ,
- (c) $(C=O)R^{13}$,
- (d) $(C=O)OR^{13}$,
- (e) $(C=O)NR^9R^{10}$,
- (f) $S(O)_mR^{13}$,
- (g) $S(O)_mNR^9R^{10}$,
- (h) C_{1-7} alkyl which is optionally substituted by one or more R^{11} substituents,
- (i) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R^{11} substituents;
- (j) aryl optionally substituted by one or more R^8 , or
- (k) heteroaryl optionally substituted by one or more R^8 ;

 R^{17} is

- (a) H,
- (b) -OH, and
- (c) C_{1-4} alkyl;

 R^{19} is

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- (a) H,
- (b) OR^{11} ,
- (c) Oxo,
- (d) C_{1-7} alkyl which is optionally substituted by one or more ~~by one or~~ R^{11} substituents,

(e) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more ~~by one or more~~ R^{11} substituents,

- (f) aryl optionally substituted by one or more R^8 , or
- (g) heteroaryl optionally substituted by one or more R^8 ;

R^{20} is

- (a) H,
- (b) C_{1-7} alkyl which is optionally partially unsaturated and is optionally substituted by one or more R^{11} ,
- (c) C_{3-8} cycloalkyl which is optionally partially unsaturated and is optionally substituted by one or more R^{11} ,
- (d) aryl optionally substituted by one or more R^8 ,
- (e) heteroaryl optionally substituted by one or more R^8 , or
- (f) R^{20} and R^{19} , taken together, form $-CH_2-$;

wherein, "aryl" denotes a phenyl radical or an ortho-fused bicyclic carbocyclic radical having about nine to ten ring atoms in which at least one ring is aromatic;

wherein, "heteroaryl" encompasses a radical attached via a ring carbon or ring nitrogen of a monocyclic aromatic ring containing five or six ring atoms consisting of carbon and 1, 2, 3, or 4 heteroatoms, selected from oxygen (-O-), sulfur (-S-), oxygenated sulfur such as sulfinyl ($S=O$) and sulfonyl ($S(=O)_2$), or nitrogen $N(Z)$ wherein Z is absent or is H, O, C_{1-4} alkyl, phenyl or benzyl, or a radical of an ortho-fused bicyclic heterocycle of about eight to ten ring atoms derived therefrom;

het¹ is a C- or N- linked five- (5), six- (6), seven- (7), or eight- (8) membered mono- or bicyclic ring, each mono- or bicyclic ring being fully saturated or partially unsaturated, and having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen; het¹ being optionally substituted by 1-2 substituents

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selected from C₁-C₄alkyl, amino, C₁-C₄alkylamino, C₁-C₄alkyloxy, halogen -CN, =O, =S;

each k is independently 0, 1, or 2;

each m is independently 0, 1, or 2;

each n is independently 1, 2, or 3; and

provided that

when each R₄ is H, that R₁ and R₂ are not simultaneously H, CN, or -C(O)-OCH₃ or that R₁ is not CN and R₂ is not -C(O)-OC₁₋₄alkyl;

when the compound is 1,2,4,4a-Tetrahydro-cis-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione that the compound is enantiomerically enriched (-) form of (2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione; and

the compound is not 2,3,4,4a-tetrahydro-1',3'-dimethylspiro[1H 1-methylpyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2'4'6'(1'H, 3'H)-trione.

2. (Original) The compound of claim 1, wherein each R⁴ is independently

- (a) H,
- (b) halo,
- (c) SR¹²,
- (f) S(O)_mR¹³,
- (g) NR⁹R¹⁰,
- (h) NR⁹S(O)_mR¹³,
- (i) NR⁹C(=O)OR¹³,
- (j) phenyl optionally substituted by one or more R⁸,
- (k) heteroaryl optionally substituted by one or more R⁸,
- (l) cyano,
- (m) nitro,
- (n) CONR⁹R¹⁰,
- (o) CO₂R¹²,
- (p) C(=O)R¹³,
- (q) C(=NOR¹²)R¹³,

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- (s) $\text{NR}^9\text{C}(=\text{O})\text{-R}^{12}$,
- (t) C_{1-7} alkyl which is optionally partially unsaturated and is optionally substituted by one or more R^{11} , or
- (u) het^1 optionally substituted by one or more R^8 .

3. (Original) The compound of claim 2, wherein each R^4 is independently selected from NO_2 , H, Br, F, CF_3 , CN, NH_2 , $-\text{C}(\text{O})\text{-OCH}_3$, $-\text{S-CH}_3$, $-\text{S}(\text{O})_2\text{-CH}_3$, $-\text{N}(\text{OCH}_3)\text{-CH}_3$, $-\text{NH-C}(\text{O})\text{-O-}t\text{butyl}$, $-\text{NH-C}(\text{O})\text{-CH}_3$, heteroaryl optionally substituted by one or more R^8 , het^1 optionally substituted by one or more R^8 , $-\text{S}(\text{O})_2\text{-CH}_3$, or phenyl optionally substituted by one or more of NO_2 , Cl, F, $-\text{OCH}_3$, and $-\text{OCF}_3$.

4. (Original) The compound of claim 1, wherein each R^3 is H.

5. (Original) The compound of claim 1, wherein R^1 is $-\text{C}(\text{O})\text{R}^6$.

6. (Original) The compound of claim 1, wherein R^2 is $-\text{C}(\text{O})\text{R}^7$.

7. (Original) The compound of claim 6, wherein R^1 is $-\text{C}(\text{O})\text{R}^6$.

8. (Original) The compound of claim 7, wherein R^6 and R^7 form $-\text{N}(\text{R}^{17})\text{-C}(\text{O})\text{-N}(\text{R}^{17})\text{-}$ or $-\text{N}(\text{R}^{17})\text{-C}(\text{S})\text{-N}(\text{R}^{17})\text{-}$.

9. (Canceled)

10. (Currently Amended) The compound of claim 1, wherein X is $-\text{C}(\text{R}^{15})_2\text{-O-C}(\text{R}^{15})_2\text{-}$ or $-\text{C}(\text{R}^{15})_2\text{-NR}^{16}\text{-C}(\text{R}^{15})_2\text{-}$.

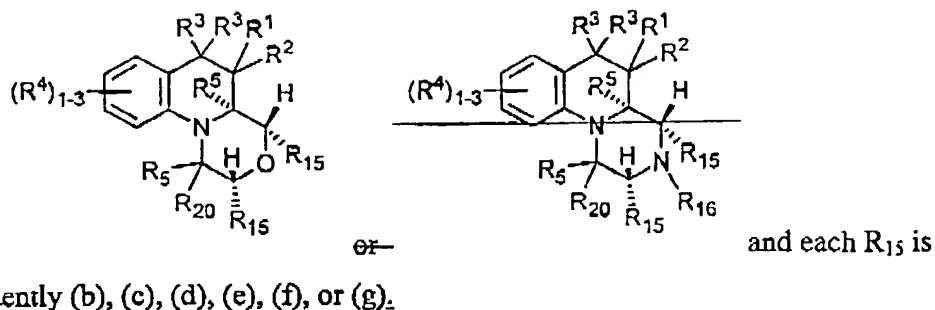
11. (Original) The compound of claim 10, wherein each R^{15} is independently H, C_{1-7} alkyl optionally substituted by one or more R^{11} substituents.

12. (Currently Amended) The compound of claim 11, wherein X is $-\text{C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-O-C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-}$ or $-\text{C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-NR}^{16}\text{-C}(\text{H})(\text{C}_{1-4}\text{alkyl})\text{-}$.

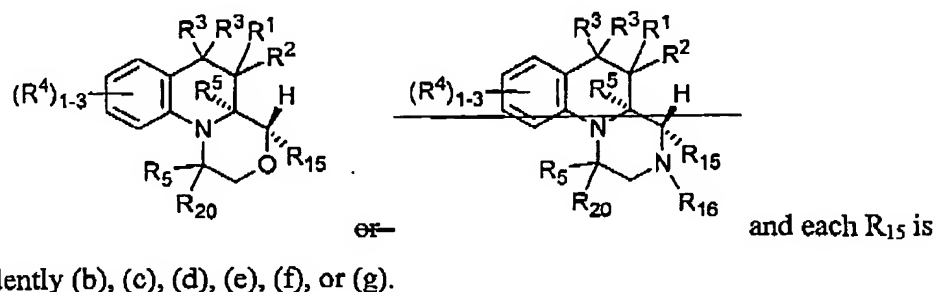
13. (Currently Amended) The compound of claim 10, wherein the compound has the formula of

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14. (Currently Amended) The compound of claim 10, wherein the compound has the formula of



15. (Original) The compound of claim 10, wherein R¹⁶ is (C=O)OR¹³ or C₁₋₇ alkyl.

16. (Original) The compound of claim 1, wherein each R⁵ is independently H or C₁₋₇alkyl.

17. (Currently Amended) A compound selected from
(2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
1,2,4,4a-Tetrahydro- 2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;
8-Bromo-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;
8-Fluoro-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

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1,2,4,4a-Tetrahydro-2,4-dimethyl-8-trifluoromethylspiro[[1,4]oxazino]4,3-a quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

1,1',2, 3',4,4',4a, 6'-Octahydro-2,4',6'-trioxospiro[[1,4]oxazino[4,3-a] quinoline-5(6H), 5' (2' H)-pyrimidine]-8-carbonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-carboxamidespiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

1,2,4,4a-Tetrahydro-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

~~8-Bromo-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]piperazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;~~

1,2,4,4a-Tetrahydro-1,4a-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

8-Bromo-1,2,4,4a-tetrahydro-cis-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-4'-thioxo-2',6' (1' H,3' H)-dione;

8-Bromo-1,2,4,4a-tetrahydro-cis-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' methyl, 3' methyl)-trione;

N-[1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinolone-5(6H),5'(2' H)-pyrimidin]-8-yl]acetamide;

tert-butyl 1,1',2, 3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinolone-5(6H),5'(2' H)-pyrimidin]-8-ylcarbamate;

8-Amino-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinolone-5(6H),5'(2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione monohydrochloride;

9-Bromo-1,2,4,4a-tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H), 5' (2' H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

8-Acetyl-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

8-Ethanone-O-methyloxime-1-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2H)-pyrimidine]-2',4',6' (1' H,3' H)-trione;

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1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylsulfonyl)spiro[[1,4]oxazino [4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylsulfinyl)spiro[[1,4]oxazino [4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-(methylthio)spiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*methyl*,3'*methyl*)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*, 3'*methyl*)-trione;

1,2, 4,4a-Tetrahydro-4-methyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;

1,2,4,4a-Tetrahydro-2-methyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*s*)-trione;

~~2,3,4,4a-Tetrahydro 1',3,3'-trimethylspiro[1*H*-pyrazino[1,2-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;~~

~~2,3,4,4a-Tetrahydro 3-methylspiro[1*H*-pyrazino[1,2-*a*]quinoline 5(6*H*),5'(2'*H*)-pyrimidine]-2',4',6'(1'*H*,3'*H*)-trione;~~

~~1,1-Dimethylethyl 1,1',2,3',4',4a,6'-octahydro-8-nitro-2',4',6'-trioxospiro[3*H*-pyrazino[1,2-*a*]quinoline-5(6*H*),5'(2'*H*)-pyrimidine]-3-carboxylate;~~

~~1,1-Dimethylethyl 8-cyano-1,1',2,3',4',4a,6'-octahydro-2',4',6'-trioxospiro[3*H*-pyrazino[1,2-*a*]quinoline 5(6*H*),5'(2'*H*)-pyrimidine]-3-carboxylate;~~

1,1',2'3'4'4'-Hexahydro-2',4'-dimethyl-1,3-dioxospiro[2*H*-indene-2,5'(6'*H*)-[1,4]oxazino[4,3-*a*]quinoline]-8'-carbonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl[1,4]oxazino[4,3-*a*]quinoline-5,5,8(6*H*)-tricarbonitrile;

8-Bromo-1,2,4-4a-tetrahydro-2,4-dimethyl[1,4]oxazino[4,3-*a*]quinoline-5,5(6*H*)-dicarbonitrile;

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~~2,3,4,4a-Tetrahydro-3-methyl-8-nitro-2'-thioxospiro[1H-pyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-4',6'(1'H,3'H)-dione;~~

9-(4-Chlorophenyl)-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-[4-(trifluoromethoxy)phenyl]spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-9-(methoxyphenyl)-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

9-(3-Chloro-4-fluorophenyl)-1,2,4,4a-tetrahydro-2,4-dimethylspiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-(3-nitrophenyl)spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,1',2,3',4,4',4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-9-yl]benzonitrile;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-[4-(methylsulfonyl)phenyl]spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

1,2,4,4a-Tetrahydro-2,4-dimethyl-9-(4-pyridinyl)spiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;

Methyl-1,1'-2,3',4,4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-9-carboxylate; and

Methyl-1,1'-2,3',4,4a,6'-Octahydro-2,4-dimethyl-2',4',6'-trioxospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-8-carboxylate;

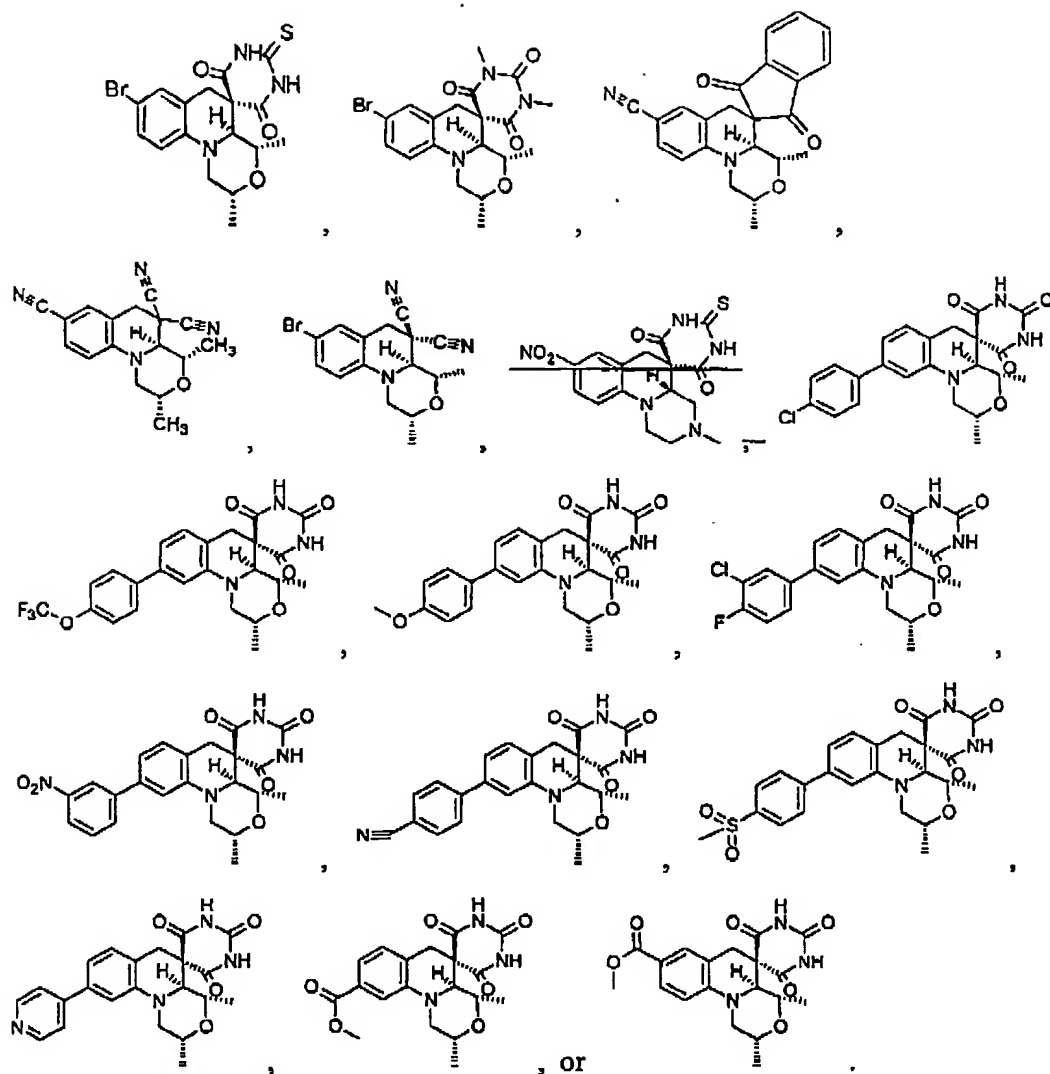
~~1,2,3,3',4,4',4a,6'-Octahydro-2',4',6'-trioxospiro[1H-pyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-8-carbonitrile monohydrochloride; and~~

~~2,3,4,4a-Tetrahydro-8-nitrospiro[1H-pyrazino[1,2-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione monohydrochloride.~~

18. (Currently Amended) A compound selected from

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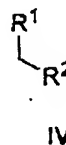
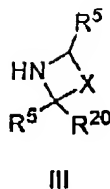
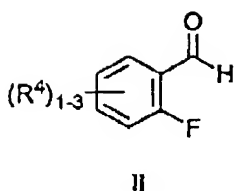
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19. (Currently Amended) A method of synthesizing compounds of claim 1 having formula I, comprising reacting an amine of the formula III with a fluoroaldehyde of the formula II in a polar, aprotic solvent, followed by methylenation with a compound of the formula IV, and thermal rearrangement in a polar, protic solvent, an aprotic solvent, or a nonpolar solvent system including ZnCl_2 .

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wherein, X, R¹, R², R³, R⁴, R⁵, and R²⁰ are as defined in claim 1 above.

20. (Currently Amended) A method for the treatment of bacterial microbial infections in mammals comprising administration of an effective amount of compound of claim 1 to said mammal.

21. (Original) The method of claim 20 wherein said compound of claim 1 is administered to the mammal orally, parenterally, transdermally, or topically in a pharmaceutical composition.

22. (Original) The method of claim 20 wherein said compound is administered in an amount of from about 0.1 to about 100 mg/kg of body weight/day.

23. (Original) The method of claim 20 wherein said compound is administered in an amount of from about 1 to about 50 mg/kg of body weight/day.

24. (Original) A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.

25. (Currently Amended) A pharmaceutical composition comprising one or more compounds of claim 1 and a pharmaceutically acceptable carrier.

26. (Original) The composition of claim 25 wherein the composition comprises an enantiomerically enriched form of a compound of formula I.

27. (Original) The composition of claim 26, wherein the composition comprises at least 50% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

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28. (Original) The compositions of claim 27, wherein the composition comprises at least 80% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

29. (Original) The compositions of claim 27, wherein the composition comprises at least 90% of one enantiomer of a compound of formula I relative to the other enantiomer of the compound.

30. (Currently Amended) A compound selected from
(2S,4R,4aR)-4-isopropyl-2-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-2,4-diethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-8-acetyl-9,10-difluoro-2,4-dimethyl-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-10-fluoro-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-2,4-dimethyl-8-[5-(trifluoromethyl)-1,2,4-oxadiazol-3-yl]-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
1,2,4,4a-Tetrahydro-2,4-dimethyl-8-nitrospiro[[1,4]oxazino[4,3-a]quinoline-5(6H),5'(2'H)-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2S,4R,4aR)-2-isopropyl-4-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2S,4R,4aR)-2-isopropyl-4-methyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-2,4-diisopropyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;
(2R,4S,4aS)-2,4-dimethyl-8-(3-methyl-1,2,4-oxadiazol-5-yl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

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(2S,4R,4aR)-8-acetyl-10-fluoro-2,4-dimethyl-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

~~(2'R,4'S,4a'S)-2',4'-dimethyl-8'-nitro-1',2',4',4a'-tetrahydro-2'H,6'H-spiro[pyrimidine-5,5' [1,4]thiazino[4,3-a]quinoline]-2,4,6(1'H,3'H)-trione;~~

8-bromo-2,4-dimethyl-10-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2R,4S,4aS)-2,4-dimethyl-8-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

(2S,4S,4aS)-4-methyl-8-nitro-2-(trifluoromethyl)-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione;

4-azido-3-iodobenzyl (2R,4S,4aS)-2,4-dimethyl-2',4',6'-trioxo-1,1',2,3',4,4',4a,6'-octahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-8-carboxylate; or

(2S,4S,4aS)-2,4-dimethyl-8-nitro-1,2,4,4a-tetrahydro-2'H,6H-spiro[1,4-oxazino[4,3-a]quinoline-5,5'-pyrimidine]-2',4',6'(1'H,3'H)-trione.